

IN THE CLAIMS:

Kindly rewrite Claims 1-19 as follows, in accordance with 37 C.F.R. § 1.121:

1. (Currently amended) A method for identifying a compound that promotes the activity capability of osteoblasts to form an extracellular matrix *in vivo*, comprising:

- (a) contacting at least one cell-osteoblast with a test compound *in vitro*;
- (b) determining an activity of the Fhl2-gene or Fhl2 protein level in the at least one cellosteoblast;
- (c) comparing the said activity determined protein level obtained in (b) to the activity of the Fhl2-gene or Fhl2 protein level in at least one control cell-osteoblast that has not been contacted with the test compound; and
- (d) selecting the test compound if the activity protein level measured in (b) is significantly different from that in the at least one control cellosteoblast.

2. (Currently amended) A-The method according to claim 1, comprising:

- (a)—contacting at least one cell with a test compound *in vitro*; wherein said Fhl2 protein level is determined by
 - (b)—measuring the level of *Fhl2* expression in the at least one cellosteoblast;
 - (c)—comparing the level of *Fhl2* expression measured in (b) to the level of *Fhl2* expression in at least one control cell that has not been contacted with the test compound; and
 - (d)—selecting the compound if the level of *Fhl2* expression measured in (b) is higher than that in the at least one control cell.

3. (Currently amended) A-The method according to claim 1, wherein said Fhl2 protein level is determined by comprising:

- (a)—contacting at least one cell with a test compound *in vitro*;
- (b)—measuring the amount of Fhl2 protein in the nucleus of the at least one cellosteoblast;
- (c)—comparing the amount of Fhl2 protein measured in (b) to the amount of Fhl2 protein in the nucleus of the at least one control cell that has not been contacted with the test compound; and

(d) — selecting the compound if the level of Fhl2 protein measured in (b) is higher than that in the control cell(s).

4. (Currently amended) A—The method according to claim 1, wherein said Fhl2 protein level is determined by comprising:

(a) — contacting a test compound with at least one cell *in-vitro*;

(b) — determining the level of interaction between Fhl2 protein and Runx2 protein in the ~~the~~osteoblast(s)

;

(c) — comparing the level of interaction determined in (b) to the level of interaction between Fhl2 protein and Runx2 protein in at least one control cell that has not been contacted with the test compound; and

(d) — selecting the compound if the level of interaction measured in (b) is significantly different from that in the control cell(s).

5. (Currently amended) A—The method according to claim 1, wherein the at least one cell is selected from the group consisting of primary osteoblasts, MC3T3-E1 cells, ROS17 cells and U2-OS cells.

6. (Previously presented) A method for preparing a compound that is useful in the treatment of a bone disease, comprising:

(a) identifying a compound by a method according to claim 1; and

(b) synthesizing the compound.

7. (Withdrawn) A compound that is useful in the treatment of a bone disease wherein the compound is capable of an activity selected from the group consisting of promoting osteoblast activity by enhancing the expression of the *Fhl2* gene, promoting the translocation of Fhl2 protein in the nucleus, modulating the interaction between Fhl2 protein and Runx2 protein, and combinations thereof.

8. (Withdrawn) A compound according to claim 7 wherein the compound is capable

of enhancing signals mediated by Rho proteins.

9. (Withdrawn) A method for the treatment of a bone disease, the method comprising:

administering a therapeutically effective amount of a medicament comprising an *Fhl2* nucleic acid selected from the group consisting of:

- (a) polynucleotides comprising the sequence as shown in SEQ ID NO:1;
- (b) polynucleotides comprising a sequence which has an identity of at least 50% to the sequence as shown in SEQ ID NO:1;
- (c) polynucleotides hybridizing to the sequence as shown in SEQ ID NO:1 under stringent conditions;
- (d) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence as shown in SEQ ID NO:2; and
- (e) polynucleotides comprising a sequence which encodes a polypeptide having an amino acid sequence which has an identity of at least 70% to the amino acid sequence as shown in SEQ ID NO:2.

10. (Withdrawn) The method according to claim 9, wherein the *Fhl2* nucleic acid is a polynucleotide encoding a polypeptide having an amino acid sequence as shown in SEQ ID NO:2.

11. (Withdrawn) The method according to claim 9 wherein the *Fhl2* nucleic acid is a polynucleotide comprising the sequence as shown in SEQ ID NO:1.

12. (Withdrawn) The method according to claim 9, wherein the bone disease is characterized by a decreased bone mass relative to that of non-diseased bone.

13. (Withdrawn) The method according to claim 9, wherein the bone disease is osteoporosis.

14. (Withdrawn) The method according to claim 9, wherein the *Fhl2* nucleic acid is

overexpressed in osteoblasts.

15. (Withdrawn) A method of diagnosing a bone disease, comprising

- (a) determining *in vitro* the level of expression of the *Fhl2* gene in tissue from an individual; and
- (b) comparing the level determined in (a) to the level of expression of the *Fhl2* gene in control tissue;

so that if the level determined in (a) is lower than that of the control, the individual is diagnosed as exhibiting the bone disease.

16. (Withdrawn) A method according to claim 15 wherein the bone disease is osteoporosis.

17. (Withdrawn) A method for developing a medicament useful for the treatment of bone diseases comprising.

a) administering a test compound to a transgenic non-human animal having a decreased level of expression of the *Fhl2* gene relative to that of the corresponding wild-type animal,

b) determining osteoblast activity,

c) comparing the activity determined in (b) to the osteoblast activity in a control animal that has not been contacted with the test compound, and

d) selecting the test compound as the medicament useful for the treatment of bone diseases if the activity measured in (b) is significantly different from that in the control animal.

18. (Withdrawn) The method according to claim 17, wherein the transgenic non-human animal is a knockout mouse.

19. (Withdrawn) A method for identifying a compound that promotes the activity of

osteoblasts, comprising:

- (a) administering a test compound to a transgenic non-human animal having a decreased level of expression of the Fhl2 gene relative to that of the corresponding wild-type animal;
- (b) determining an activity of the Fhl2 gene or Fhl2 protein;
- (c) comparing the activity determined in (b) to the activity of the Fhl2 gene or Fhl2 protein in a control animal that has not been contacted with the test compound; and
- (d) selecting the test compound if the activity measured in (b) is significantly different from that in the control animal.